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Pain mechanisms in causalgia

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SYNOPSIS A study of the clinical features of causalgia and the central neuronal effects of injuries to peripheral nerves suggests that causalgia is the functional expression of the intensity of the retrograde neuronal reaction in which pools of dorsal horn neurones become converted into foci of abnormal activity. These foci initiate a chain reaction along transmission pathways as far centrally as the cortex, causalgia being the terminal effect of this disorderly activity on the sensorium. This is the basis of the 'turbulence hypothesis' introduced to account for the pain.

On occasion trauma to a peripheral nerve is followed by spontaneous pain in the hand or foot which is so severe and compelling that it becomes the dominant feature of the injury, incapacitating the patient and sometimes converting him into a nervous wreck. This pain is worthy of special attention because of its disabling nature and because of the distinctive clinical features associated with the lesion which have earned for the condition a special identity and name, causalgia (Mitchell, 1867).

The present incomplete state of our knowledge permits no easy understanding or ready explanation of the genesis of this distressing condition. This paper concerns the continuing search for the mechanisms operating and the manner in which they produce their unpleasant and harmful effects.

The clinical observations on which the present study is based were reported in detail by Sunderland and Kelly in 1948 and the literature on causalgia updated by Sunderland in 1968. Here the clinical features characteristic of the condition will be reviewed and their significance in relation to possible aetiological factors examined. Finally, because causalgia so often persists after the offending nerve lesion has been isolated from the nervous system, the findings have a more general application in that they provide a clue to mechanisms of pain production in those cases in which pain persists long after the initial peripheral lesion has resolved.

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CLINICAL FEATURES OF CAUSALGIA

IDENTITY OF NERVE INJURED In the great majority of cases causalgia follows lesions of the medial cord of the brachial plexus, the median nerve, or the sciatic nerve. This finding cannot be explained on the grounds that these nerves are more frequently injured than others. These three tracts must, therefore, possess features which render them especially liable to causalgia. The following two features appear to be significant in this respect.

1. These nerves carry the bulk of the long sensory nerve fibres destined for the innervation of the hand and the foot.

2. Forty per cent to 70% of the postganglionic sympathetic fibres to the upper limb are contained in the lower trunk of the brachial plexus (Sunderland and Bedbrook, 1949). The majority of these run peripherally in the medial cord and median nerve and are destined for the hand. In the leg the bulk of the sympathetic fibres pass to the foot by the sciatic nerve and its tibial division.

LEVEL OF INJURY With few exceptions, causalgia is confined to those nerve lesions which are situated above the elbow and the knee. This finding cannot be attributed to differences in the fibre composition of the nerve at proximal and distal

levels because the sensory and sympathetic fibres for the hand and foot continue in the nerve trunk as far as the wrist and ankle respectively.

SEVERITY OF INJURY This complication is more common in lesions caused by high velocity missile wounding where the nerve is known to have been subjected to rapid and violent deformation. At the same time, they are lesions which usually recover spontaneously, even though this recovery may be incomplete. While causalgia is rare after peripheral nerve severance, it is known to follow division of all nerves in the limb occasioned by amputation.

ONSET OF PAIN Some patients insisted that the pain in the extremity commenced at the moment of wounding. Thus, a soldier will say that he thought he was hit in the foot or the hand. Others, while lacking a clear memory of events at the time of wounding, nevertheless claimed that, though they were not certain if the pain commenced immediately, were clear that it undoubtedly did so within an hour or two. For some the whole limb went numb at the moment of wounding and pain was felt as the numbness wore off in a few hours or a few days. Others who had been unconscious for some weeks complained of pain on recovery of consciousness. The significant observation is that the pain of causalgia commonly appears either immediately or too soon after the injury to be attributable to pathology which develops relatively slowly—for example, perineural and intraneural fibrosis and neuroma formation. Importantly, the pain is present despite the fact that the lesion is clinically complete, and well before the onset of spontaneous recovery.

CHARACTERISTICS OF PAIN The pain is spontaneous and, though waxing and waning and subject to exacerbations, it is continuous. These features suggest a self-sustaining excitatory state. The quality of the pain tells us little about the aetiology. The continuous burning pain is usually felt superficially in the skin of the palm, sole, and digits. This points to involvement of cutaneous sensory mechanisms or a vascular factor. The stabbing, crushing, bursting, tearing pains are felt more deeply and indicate involvement of deep sensory mechanisms.

It has been suggested that the sensation of heat may be due to a coincidental increase in the circulation. Usually, however, the burning quality has no relation to the temperature of the skin and patients are often surprised when, on touching the affected area with a finger, the skin is not hot. The evidence suggests that the abnormal sensation of heat is due to a disorder of sensory mechanisms rather than of vascular control.

The exquisite sensitivity and hyperpathia which develop during recovery is more marked than that found in the field of a nerve at a time when regenerating processes have reached the skin.

In most patients the pain gradually subsides and vanishes within six months; it rarely persists for more than a year. This suggests that whatever changes are responsible are either fully reversible or are gradually corrected by readjustment or adaptation.

EASE WITH WHICH PAIN IS AGGRAVATED BY ACTIVITY ELSEWHERE IN NERVOUS SYSTEM Clearly those abnormal patterns of cortical activity that are interpreted as pain must share the cortex with other patterns of activity and these may modify the threshold, intensity, quality, and other characteristics of the pain. A great variety of stimuli may intensify the pain or provoke severe attacks but they commonly fall into two classes: (1) anything which increases the activity of the limb; (2) anything which increases the activity of the central nervous system. In fact, anything which disturbs the *status quo* in sensory neuronal pools may intensify the pain. Incidents which may cause considerable distress fall into somatosensory, auditory, visual, and emotional categories. Most of the visual and auditory stimuli which aggravate the pain probably do so by way of the emotional reaction associated with the incident.

Any form of stimulus to the limb, such as mechanical stimuli, heat, cold, muscular activity, and movement, may increase the pain. Jarring the bed, a sudden reflex movement, or touching the part may cause distress and, if hyperaesthesia be severe, even a light touch, such as a fly alighting on the affected area, may cause intense agony. As a result, the patient avoids movements and takes particular care to protect the painful limb

from being knocked or even touched. Venous congestion caused by the limb hanging in a dependent position intensifies the pain, and the patient avoids such positions by appropriately posturing the limb.

The response to temperature changes varies. Many patients are emphatic that heat increases and cold eases the pain, while others claim that warmth gives relief and cold makes it worse. Some patients are indifferent to changes in temperature. In yet another group, the pain is intensified by both warmth and cold. Regardless of the effect of temperature changes on the pain, the majority of patients benefit from cool moist conditions and resort to wrapping the affected hand or foot in moist cloth, or to immersing it in water in order to obtain relief. In these cases it is the moisture and not a change in temperature which brings relief.

The pain may be exacerbated by loud and unexpected noises—for example, noise of aircraft, shelling, radio, rattling of crockery, tearing of paper, scraping a chair, while examples of disturbing visual stimuli are a sudden burst of sunlight or switching on the light in a darkened room.

Disturbing emotional factors include looking from a height, witnessing a mishap in the street, the excitement induced by watching a sporting event or movie, and emotional disturbances associated with anxiety, fear, worry, anger, arguments, and fatigue. These incidents may cause such intense suffering that the patient shuns all company and is ultimately converted into a recluse. Upper limb causalgia is aggravated to a greater degree by such stimuli than is causalgia of the lower extremity. A possible explanation is that the sensory centres devoted to the hand are more extensive than those related to the foot.

DISTRIBUTION OF PAIN In every case, the pain is felt in the hand or the foot and involves the distribution of the injured nerve. When severe, the pain always spreads to involve adjacent territories.

TROPHIC CHANGES In painless nerve lesions, trophic changes are marked only when denervation is complete and prolonged. On the other hand, despite the fact that the causalgic lesion is incomplete, trophic changes constitute a striking feature of the condition. They are rarely absent, appear earlier, are more severe, and are more likely to result in irreversible changes in the peripheral tissues. They vary in nature and degree and affect the skin, subcutaneous tissues, bones, and joints.

OBSERVATIONS BASED ON SURGICAL TREATMENT OF CAUSALGIA The long history of the changing surgical attacks on causalgia has provided valuable information from which it is possible to draw deductions as to the level at which the pain is generated. Relief is only occasionally obtained by nerve block, by infiltrating the injured segment of the nerve with a local anaesthetic or by neurolysis. Despite the occasional success, neurotomy has now been discredited, for it rarely brings relief and is not justified because spontaneous recovery is the usual outcome in these cases. The history of posterior rhizotomy is one of repeated failure.

The results of blocking and surgical procedures on the nerve indicate that the source of the pain is situated further centrally in the central nervous system.

INDICATIONS OF SYMPATHETIC INVOLVEMENT AND RESULTS OF SYMPATHECTOMY The affected hand may be cold and clammy or warm and dry. Many patients claim that the affected extremity sweats more than its fellow, whereas in others the affected hand is completely dry. Causalgia may occur in the presence of an increased, diminished or normal vasomotor tone. The pain, however, appears to be the same regardless of the nature of the blood flow, which suggests that disturbances of vasomotor function are not the cause of the pain. Neither from the disturbances of sweat secretion nor from alterations of blood flow is there any evidence which definitely implicates the sympathetic system as a factor in causalgia. Sympathetic block, however, is dramatic in its effects, relieving the pain in all but the stubborn case. The relief is usually temporary but may be permanent. Temporary relief is the cue for sympathectomy.

ORIGIN OF PAIN IMPULSES

Three possible sites have been suggested for the origin of the pain impulses: (1) the peripheral

tissues where the pain is felt; (2) the damaged segment of the nerve, and (3) the central nervous system.

PERIPHERAL TISSUES The essential feature of the peripheral hypothesis is that the cutaneous area in which the pain is felt is the source of pain-producing impulses. These impulses could originate in three ways.

1. As the result of the conjunction of sympathetic and sensory fibres at their terminations, such artificial synapses resulting from ischaemia, oedema, and the associated nutritional disturbances.

2. From the release of pain-producing vasodilator products into the tissues of the skin as the result of antidromic impulses initiated at the site of injury by the chronic irritation of sensory nerve fibres and/or activity at artificial synapses which develop in the damaged segment.

3. From the formation and accumulation of pain-producing substances elaborated in the peripheral tissues as the result of vasoconstriction and ischaemia secondary to the irritation of vasomotor nerve fibres in the injured segment. These pain-producing substances are believed to reduce the threshold to stimulation of sensory receptors giving a state of cutaneous hyperaesthesia, irritate sensory endings, and set up impulses which discharge centrally to be interpreted as pain.

The beneficial effects of sympathectomy are attributed to the washing away of the irritative substances and the interruption of vasoconstrictor pathways on which abnormal vasomotor functioning and the painful state are based.

The 'peripheral' hypothesis is open to the following objections.

Causalgia occurs in phantom limbs where the peripheral component is missing.

It fails to account for the causalgia which occurs after severance of the nerve, and that which persists after resecting the damaged segment or blocking the nerve below the lesion; here there can be no sensory feedback from the periphery.

The immediate onset of pain cannot be explained in terms of pathology which takes some time to develop.

Though burning pain is a characteristic feature of causalgia, patients often complain of deep pain which they variously describe as tearing, crushing, or gnawing. It is, therefore, clear that sensory fibres other than those serving the skin may be involved.

The relief afforded by sympathetic block and sympathectomy is unlikely to be due to the washing away of pain-producing substances because in many of these patients a state of vasodilatation obtains before the operation, and the circulation through the limb is already increased.

Vasospasm as an aetiological factor has been rejected for the following reasons:

If sympathectomy produces its beneficial effects by correcting the vasospasm, why does the vasodilatation achieved by methods other than the interruption of sympathetic pathways fail to relieve the pain?

In many cases there is no vasospasm but vasodilatation instead. The relief that follows sympathectomy in these cases cannot be attributed to vasodilatation because this condition already existed before the operation.

The vasodilatation after sympathectomy is transitory, vasomotor tone returning as the smooth muscle of the vessel wall becomes sensitized to circulating agents. Despite this, the pain is usually permanently cured by the operation.

DAMAGED SEGMENT OF NERVE Pain impulses could originate at the site of nerve trunk damage in several ways.

Changes caused by the injury could distort, but not block, conduction along individual fibres.

Scarring and neuroma formation could create a trigger point generating impulses which travel centrally in sensory fibres to be interpreted as pain. As long ago as 1930 Adrian had shown that the excitability at the end of a severed nerve is sufficiently high to cause spontaneous discharges and that, in this respect, sectioned sensory fibres were more effective impulse generators than sectioned motor fibres.

It has been claimed that any injury which leads to failure of the insulating properties of the nerve sheath permits impulses passing along a fibre, or in a group of fibres, to spread to excite quiescent neighbouring fibres or to modify their activity (Uexküll, 1894; Katz and Schmitt, 1940, 1942; Renshaw and Therman, 1941; Tasaki, 1950).

Pathologically altered regions of an injured nerve may be followed by the formation of artificial synapses which permit activity to pass from motor to sensory fibres, thereby leading to widespread central and peripheral effects (Granit *et al.*, 1944; Granit and Skoglund, 1945a,b; Skoglund, 1945). In the proximal part of the limb, motor, sensory, and sympathetic fibres for the hand and the foot are scattered and intermingled in the several funiculi constituting the nerve trunk (Sunderland, 1945); this arrangement would favour the formation of artificial synapses. Studies of such artificial synapses have shown that sensory nerve fibres—and, in particular, pain fibres in the C group—have a lower threshold to stimulation than other fibres and that they are readily excited by fibre interaction (Skoglund, 1942; Granit *et al.*, 1944).

It has been postulated that these artificial synapses permit efferent impulses in adjacent sympathetic nerves to be relayed across to fine sensory fibres and that causalgia is the result of abnormal activity originating in this way (Doupe *et al.*, 1944; Nathan, 1947; Barnes, 1953; Richards, 1967). The relief after sympathectomy is attributed to the interruption of offending sympathetic efferent fibres. Supporting this concept is the claim that, in order to be fully effective, the injured segment of the nerve should be included in the territory denervated by the sympathectomy (Allbritten and Maltby, 1946; Ulmer and Mayfield, 1946); this has been denied by others (Kirklin *et al.*, 1947).

High velocity 'near miss' missile wounding could selectively damage the large myelinated fibres, thereby resulting in an imbalance between the different fibre groups constituting the nerve. This is the basis of the fibre dissociation concept of Noordenbos (1959) and the gate control theory of Melzack and Wall (1965, 1968), both of which postulate that whenever fast conducting large fibres are proportionately reduced in number a state of imbalance results in which the spinal cord receives an excess of slowly conducted impulses.

According to Noordenbos (1959), high velocity missile wounding favours the destruction or disruption of fibres possessing a well-developed myelin sheath, while those with little or no myelin escape serious involvement. Any stimulus to the region supplied by such an injured nerve would result in abnormal discharges in which slowly conducted impulses would predominate. Moreover, with the reduction or loss of an inhibitory action of the fast conducting fibres, the passage of this abnormal pattern of slow conducted impulses centrally would be facilitated and it is the central activity generated by this abnormal afferent inflow which is the basis of causalgia.

The 'gate control theory' is a refinement of the fibre dissociation concept in that it postulates facilitatory and inhibitory mechanisms in the substantia gelatinosa of the spinal cord in which fine and large sensory fibres play opposing roles in influencing onward transmission through the dorsal horn. The lesion in causalgia is postulated to be one which selectively damages the large myelinated sensory fibres. This disturbs the balance in favour of fine fibre activity which, now unopposed, 'opens the gate'. Small fibre traffic through the system is thereby increased and pain results. Conversely, stimulating large fibres 'closes the gate' and reduces or stops the pain. This is the basis of the therapeutic use of large fibre stimulation (peripheral nerve and dorsal spinal column) for the relief of intractable pain.

In a later paper Melzack (1971) elaborated on the central control trigger mechanism by proposing that part of the brain stem reticular system exerts a tonic inhibitory effect on transmission at all synaptic levels of the somatic projection system. He then argued that the loss of the sensory input after a nerve injury leads to a decrease in this tonic inhibition, the overall effect of which is to release self-sustaining activity at all synaptic levels that can be triggered repeatedly by discharges from surviving nerve fibres. Pain occurs when the central activity developing in this way exceeds a critical level.

COMMENT While the damaged segment of the nerve may be the source of the pain in some cases, it cannot be responsible in others for the following reasons.

The repeated failure in many hands of high nerve block and neurotomy, and posterior rhizotomy.

Resection of the damaged segment of the nerve trunk has proved equally unsuccessful despite the fact that this operation removes any trigger

point as well as the afferent and efferent component of any artificial synapse.

The pain commences at a time when the nerve lesion is complete, at least physiologically. Sensory fibre imbalance would not be operating at this time, while intraneural fibrosis and the formation of neuromas and artificial synapses involve pathology with a developmental time scale which is inconsistent with the immediate onset of pain that is so characteristic and dramatic a clinical feature of many cases of causalgia.

Though 'fibre dissociation' and the 'gate control' theories account for some of the features of causalgia they leave unexplained: the immediate onset of pain at the time of wounding; the spontaneous pain which occurs in the absence of any external stimulus; the occurrence of causalgia in physiologically and anatomically complete nerve lesions; the causalgia which follows the avulsion of cervical spinal nerve roots when all fibres, small and large, have been torn from the cord. Reports are now appearing from several laboratories which question some features of the gate control theory (Iggo, 1972; Schmidt, 1972; Denny-Brown *et al.*, 1973; Nathan and Rudge, 1974).

The evidence points to causalgia of immediate onset having a central, and not a peripheral, origin.

CENTRAL FACTOR IN CAUSALGIA Livingston (1944) attributed the pain to self-sustaining abnormal activity generated in the internuncial neuronal pool of the cord by the peripheral injury. The pathological basis of this abnormal activity was left unexplained. To provide this missing link it is here proposed that causalgia is the functional expression of the intensity of the retrograde neuronal reaction which follows nerve damage.

RETROGRADE NEURONAL REACTION TO PERIPHERAL NERVE INJURY. Section of axons causes changes, which are now well documented, in the structure and function of parent cell bodies. The end result of these retrograde effects may be cell necrosis, complete recovery, or the persistence of a residual defect that impairs the efficiency of the cell. The extensive literature on this subject has been reviewed by Sunderland (1968) and Lieberman (1971) and reference should be made to these sources for confirmation of the statements which follow. More recent references are included here.

Section of an axon does not invariably result in retrograde changes in the parent cell. Why some cells should be affected and others in the same functional group escape is not known.

Affected neurones recover rapidly after mild damage to the nerve but after a severe injury recovery may be delayed for several months.

The greater the violence to the nerve the more intense the retrograde reaction; thus it is more intense when the nerve is avulsed than when it is cut or ligated. By using graded degrees of violence in stretching nerves, it has been shown that the reaction is proportional to the violence. The intensity of the reaction also increases with the length of the nerve destroyed.

The intensity of the reaction varies inversely with the distance of the lesion from the cell body. Thus the reaction is greater after proximal than after distal lesions, the neurones innervating the most distal segment of the limb being the most severely affected.

Estimates of the number of cells perishing after nerve division vary from 6 to 83%.

The reaction is more severe in sensory than in motor cells; this is especially so for the small cells of the spinal ganglia.

There could be retrograde neuronal changes that can not be detected by conventional techniques but which are sufficient to disturb or arrest the function of the cells.

After nerve section distal to the dorsal root ganglion, the neurones of the ganglion begin to discharge spontaneously after the third day and reach a steady state of slow spontaneous discharge a few days later (Denny-Brown *et al.*, 1973).

Section of sympathetic fibres is also followed by a retrograde reaction in the parent cells.

TRANSYNAPTIC REACTION TO PERIPHERAL NERVE INJURY Transynaptic changes, including cell degeneration, are commonly observed in experimental neurology and probably play a large part in neuropathology (see Sunderland, 1968). The posterior root fibres branch freely before ending in contact with the neurones of the posterior horn of grey matter. If a sensory ganglion cell suffers as the result of a peripheral nerve injury, these branches are also affected. This is followed by changes in the cells with which they have communicated. In Clarke's column, transynaptic

degeneration of cells which have been partially or wholly bereft of synaptic contacts has been frequently observed. Less is known about changes in the finest fibres carrying pain impulses because their connexions are difficult to demonstrate. After nerve section, however, the casualty rate among small spinal ganglion cells is many times greater than among large neurones, while a severe loss of both cells and fibres in the substantia gelatinosa has also been observed. For these reasons, transynaptic changes should be expected on the pain pathway after peripheral nerve section.

Depression and failure of synaptic transmission, abnormalities in the pattern of synaptic activity, and unfavourable effects on integrative functions have been described for neurones during the period of chromatolysis.

DISCUSSION

When these retrograde effects of nerve injury are examined in relation to the clinical features of causalgia some interesting correlations emerge.

The severity of the reaction is influenced by three main factors: (1) it is more intense in sensory than in motor neurones; this is especially so for the small cells of the spinal ganglia; (2) the closer the lesion to the spinal ganglia the more severe the reaction; (3) the severity of the reaction increases with the severity of the injury.

The occurrence of causalgia is also related to three factors: (1) it follows damage to the main sensory paths to the hand and foot; (2) it more commonly follows high than low injuries and is clearly related to the proximity of the lesion to the parent neurones; (3) most cases are due to high velocity missile wounding and so are related to the amount of sudden disrupting violence to which the nerve is subjected.

Causalgia, however, cannot be a manifestation only of chromatolysis in spinal ganglia for, if it were, rhizotomy would cure it, which it fails to do. The clinical evidence suggests that causalgia is the effect of the spread of the damage to the central nervous system, distress or death of the sensory ganglion cells inducing a reaction in the central cells with which they are connected. The elimination of some dorsal horn cells and the malfunctioning of others, together with related changes at synapses, could disorganize and impair the functions of whole groups of neurones, thereby creating hyperactive foci of abnormal activity in the cord which could become self-sustaining. These structural changes and functional disturbances in the cord could, in turn, initiate a chain reaction inducing similar changes along transmission pathways as far centrally as the cortex itself, causalgia being the terminal effect of this disordered activity on the sensorium.

While normal and abnormal extraspinal influences play their part in precipitating and perpetuating this central activity to give hyperaesthesia and pain, the essential feature becomes the disorganized intraspinal focus of abnormal hyperactivity which, with time, may shift from the cord to higher centres. Such hyperactive foci could, in the absence of any normal or abnormal input, come to discharge spontaneously of their own accord. This would explain the spontaneous pain in causalgia. The extension of the hyperaesthesia and pain beyond the limits of the territory served by the injured nerve could be due to the gradual spread of the disturbance to involve wider and wider areas of the cord. Finally, if these central foci be converted into self-sustaining hyperirritable foci, and assume a measure of permanence, spontaneous pain would become more persistent and more difficult to eradicate until a stage would be reached when any surgical attack on sensory pathways is bound to fail. These points are illustrated in the following case history.

CASE HISTORY A jockey was thrown from a horse on 16 September 1933 and sustained a fracture of the mid-thoracic spine with complete and permanent paraplegia. He subsequently developed a persistent distressingly severe pain in a phantom left foot. Despite the traumatic transection of the cord, a cordotomy was performed in January 1944 to relieve his pain, presumably on the grounds that the damaged cord was the site of abnormal discharges responsible for the pain. This cordotomy brought no relief. In October 1945 the patient came under the care of the late Mr. Hugh Trumble, with whom I was associated at the time. Gutiérrez-Mahoney's (1944) paper on cortical excision for the relief of intractable pain had been published the year before and on the basis of his findings it was decided to excise the leg area of the sensory cortex in the hope of relieving the patient's pain. This was done under local

anaesthesia on the morning of 4 October 1945. As the cortex and subjacent white matter representing the leg area were being removed, the patient exclaimed: 'What a relief to get rid of that pain'. His last words on leaving the theatre were: 'It is just wonderful, I just hope that it will stay like it'. Regrettably, the relief was only temporary, for after a few months the pain returned with its old intensity.

True causalgia is rare in civilian practice, for this is a complication not only of high velocity missile wounding but of such wounding under conditions of combat stress. It might be that, when the nervous system is subjected to such stressful conditions, injuring a nerve which provides the major sensory inflow from the limb may facilitate the development of those central effects which are claimed to be the basis of causalgia.

In most cases, the hyperaesthesia and pain gradually diminish and finally disappear. This would occur as neurones gradually recover and the disorderly activity finally subsides.

The Oxford Dictionary defines 'turbulence' as violent commotion, agitation, or disturbance. Turbulence therefore seems an appropriate term to apply to those foci of disorderly activity in the spinal cord and further centrally that are claimed to be responsible for the pain of causalgia. In contradistinction to fibre dissociation, such a hypothesis focuses attention on the consequences of the retrograde neuronal and transynaptic changes that are known to follow peripheral nerve injury.

The 'turbulence hypothesis' is consistent with: (1) the higher incidence of causalgia in lesions of the medial cord of the brachial plexus, median, and sciatic nerves; (2) the higher incidence of causalgia in nerve lesions above the elbow and knee; (3) the mechanism of wounding; (4) the immediate onset of pain; (5) the characteristics of the pain—spontaneous, continuous, and fluctuating in intensity; (6) the hyperaesthesia; (7) the extension of pain to neighbouring areas; (8) the ease with which a great variety of stimuli—for example, mechanical, thermal, visual, auditory, emotional—summate at central levels to raise the activity of disturbed sensory neuronal pools to intensify the pain or precipitate an attack; (9) the manner in which the pain gradually subsides and goes; (10) the occurrence of causalgia in severe traction injuries of the brachial plexus and of intercostal nerves in thoracotomy, both of which involve the tearing of axons close to the spinal cord; (11) the failure to relieve the pain by interrupting sensory pathways external to the cord.

The turbulence hypothesis leaves unexplained the dramatic relief which usually follows blocking or surgically interrupting the sympathetic supply to the limb. Such relief has been attributed to the interruption of (1) afferent fibres from the limb which take an aberrant course to the posterior roots by traversing the ganglionated sympathetic trunk (such somatic afferent fibres have not been demonstrated); (2) afferent fibres from the viscera which are known to travel *via* the sympathetic trunk on their way to the posterior nerve roots and the spinal cord where they converge on the same cells that receive sensory fibres from the skin (Pomeranz *et al.*, 1968). Discharges over this system could summate with those entering from the limb and lead to pain.

However, if the severance of these two afferent pathways in the sympathectomy were responsible for the relief then their severance in posterior rhizotomy should be equally successful, but this is rarely so. The possible role of sympathectomy in relation to artificial synapses has already been discounted. One can only speculate that sympathectomy introduces some central factor which results in the suppression of the hyperirritable foci created by the nerve lesion.

Another difficulty concerns the absence of pain in peripheral nerve injuries where the severity of damage might have been expected to lead to changes of the type claimed to be responsible for causalgia. A further difficulty is that the hypothesis fails to explain why causalgia develops more commonly in partial than in complete lesions. However, the present state of knowledge regarding these retrograde effects is so incomplete that it provides only a clue to the structural and functional basis of the turbulence hypothesis which will probably have to be modified as further and more extensive investigations reveal details of the obscure processes involved. In the meantime, some theoretical synthesis of the data already available is justified if only to provide a challenge to the imagination and to experimental initiative directed to new and more fruitful lines of investigation.

Finally, the results of this study of causalgia

may have a more general application by offering a clue to the persistence of pain associated with a wide variety of peripheral lesions long after the initial offending lesion has been corrected. It also explains why attacks on neural pathways external to, and within, the central nervous system for the relief of long-standing intractable pain so often fail.

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